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# SmartNotes

## Post-viral syndrome: Tackling the COVID-driven increase in AMR starts in the laboratory

***At the height of the COVID-19 pandemic, antimicrobial stewardship, understandably, fell down the medical community's list of priorities. But with the virus now largely under control, it is time to refocus, reassess, and double down on tackling antimicrobial resistance (AMR) – before it is too late.***

In 2021 we highlighted concerns that antibiotic use was on the rise as doctors struggled to fight the clear and present danger of SARS-CoV-2. This has since been documented in the literature. One meta-analysis of 115 studies from across the United States, Europe, Asia, and the Middle East showed that around 75% of people with COVID-19 in the first six months of the pandemic received antibiotics, despite an overall bacterial co-infection rate of 3.5% and a secondary bacterial infection rate of 14.3%.[1]

Data shows this has contributed to an increased incidence of AMR,[2-4] and the US' Centers for Disease Control and Prevention (CDC) reported an "alarming rise" in resistant organisms between 2019 and 2020.[5] Without a concerted effort to stem the tide, we could be facing a public health crisis an order of magnitude more deadly than SARS-CoV-2.

In this SmartNote, we look at how COVID-19 care has affected AMR, the ever-growing importance of stewardship programs, and how combining cutting-edge diagnostics with advanced treatments has the potential to avoid a healthcare crisis, and save lives in the coming years.

### AMR and stewardship

According to the World Health Organization, drug-resistant diseases cause at least 700,000 deaths a year, and could lead to 10 million annual fatalities by 2050.[6] These figures, from a 2019 report, are staggering, and yet they do not even account for the increased incidence of AMR witnessed during the COVID-19 pandemic.

Of course, some degree of antimicrobial resistance will always be inevitable, and ending humanity's reliance on life-saving antimicrobials is not an option. The only feasible approach, then, is slowing the progression of AMR through stewardship programs, which tend to follow the five strategic objectives set out in the WHO Global Action Plan:[7]

1. Strengthening knowledge through surveillance and research
2. Reducing the incidence of infection
3. Optimizing the use of antimicrobial agents
4. Improving awareness and understanding of AMR
5. Developing the economic case for sustainable investment and increasing investment in new medicines, diagnostic tools, vaccines, and other interventions

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In healthcare settings, stewardship entails ensuring agents are only used when they are needed, and for the shortest time possible. It is about optimizing clinical outcomes while minimizing the unintended consequences of antimicrobial use. Yet, in retrospect, more often than not the use of antimicrobials may not align with those goals. In a cross-section study of 1566 patients at 192 hospitals, antimicrobial use deviated from recommended practices for 55.9% of patients who received antimicrobials for community-acquired pneumonia or urinary tract infection present at admission who received fluoroquinolone or intravenous vancomycin treatment.[8]

Examples include:

- Prescribing antibiotics unnecessarily, such as in a case of COVID-19 with no evidence of bacterial infection, for example.
- Prescribing a broad-spectrum antibiotic when a narrow-spectrum agent would be effective.
- Prescribing doses at levels higher or lower than needed to fight the infection.
- Prescribing a treatment course that is longer or shorter than needed to fight the infection.
- Failing to optimize treatment approaches when microbiological culture data become available.

According to WHO, the “misuse and overuse of antimicrobials are the main drivers in the development of drug-resistant pathogens”.[9] But microbiology laboratories have access to reliable, accurate, diagnostics with the power to guide appropriate agent selection and dosing regimens – all of which has the potential to be game changing:

- Microbiological data can help confirm the existence of an infection prior to and during treatment, making sure patients only receive antibiotics when they need them.
- They can also distinguish between bacterial, viral, and parasitic infections, ensuring antimicrobials are only used when necessary.
- Culture results and antimicrobial susceptibility testing (AST) can help narrow the choice of drug, allowing clinicians to step down from broad-spectrum agents.
- Minimum inhibitory concentration (MIC) results determine the lowest concentration of an antimicrobial that will inhibit the visible growth of the microorganism in question. This enables clinicians to prescribe the lowest dose for the shortest period, ensuring the best patient outcome without unnecessarily contributing to further AMR.

It all adds up to the more judicious prescribing of antimicrobials that not only fights the spectre of AMR, but improves patient outcomes and results in the more efficient use of resources.

One systematic review, for example, found hospitals implementing stewardship programs were able to reduce length of stay by up to 22 days. The average annual stewardship-associated cost savings were $435,000 per hospital in the United States, €41,500 in the Euro zone, and £144,000 in the United Kingdom.[10]

## AMR and COVID-19

The advent of COVID-19 changed processes and priorities almost overnight. As hospitals were overwhelmed with patients, and with historical viral influenza data suggesting bacterial co-infection would be prevalent to guide them, the medical community resorted to the wide-spread empiric use of broad-spectrum antibiotics, or prescribing agents without confirming the presence of a bacterial infection (see figure 1).[1]

### Antibiotic prescribing in patients with COVID-19 vs. estimated co-bacterial infection up to 9/6/2020 (n=30,623)

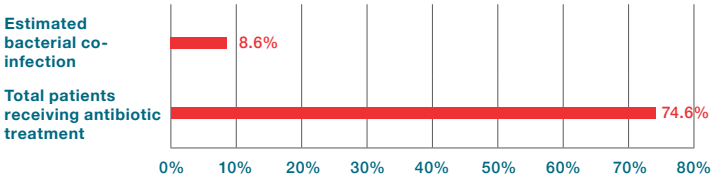


Figure 1: Antibiotic prescribing in patients with COVID-19 vs. estimated co-bacterial infection up to June 2020 across 154 studies[1]

Leading figures have been voicing their concerns on the AMR potential impact of the overuse of antimicrobials for some time, and have since been vindicated. A special report from the CDC published this year, for example, warned of a significant increase in resistant hospital-onset infections and resulting deaths during the first year of the pandemic (see fig 2).[5]

### Increase in resistant infections starting during hospitalization between 2019 and 2020)

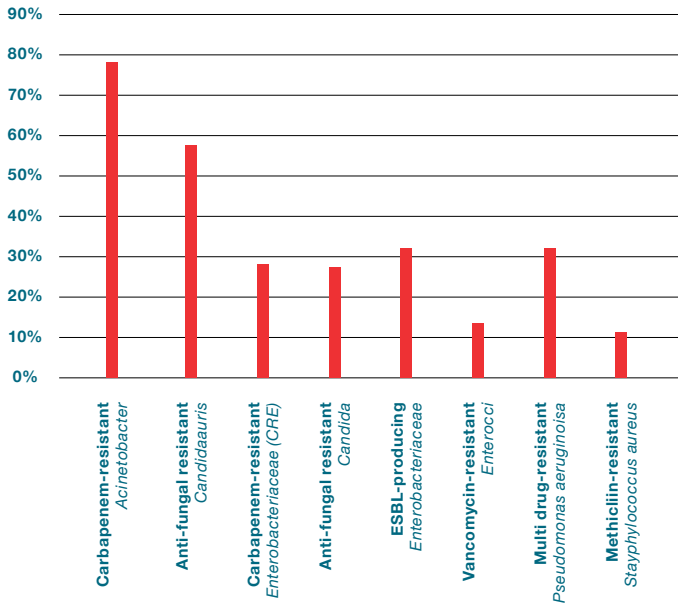


Figure 2: Sample of COVID-19 impact on antimicrobial-resistant bacteria and fungi during 2020 (CDC data)[5]

In Europe the number of reported cases of *Acinetobacter* spp. infections showing resistance more than doubled (121%) in 2021 compared to the average for 2018–2019, according to the European Centre for Disease Prevention and Control. The number of *K. pneumoniae* cases resistant to carbapenems reported by laboratories that continuously reported data from 2017 to 2021 increased by 31% in 2020, and by a further 20% in 2021.[13]

> *"A growing body of evidence suggests AMR may be increasing following antimicrobial prescribing in COVID-19 patients,"*
>
> Antimicrobial resistance (AMR) in COVID-19 patients: A systematic review and meta-analysis.[1]

## Where do we go from here?

The evidence is clear. The empiric use of antibiotics in hospitalized patients with SARS-CoV-2 accelerated AMR and threatened global health security. With the mounting body of evidence on how to best manage these patients, a refocus on the other pending pandemic, AMR, is top of mind.

> *"These setbacks can and must be temporary. The COVID-19 pandemic has made it clear—prevention is preparedness. We must prepare our public health systems to fight multiple threats, simultaneously. Because antimicrobial resistance will not stop,"*
>
> CDC Special Report: COVID-19 U.S. Impact on Antimicrobial Resistance.[5]

Newer, more efficacious agents with more preferable side effect profiles, such as novel beta lactams and beta-lactamase inhibitor (BLI) combinations, are an important part of the solution. Such new agents, however, cannot fight the AMR crisis alone. Rather, their use must be guided by advanced, reliable diagnostics.

Effective stewardship relies on laboratories utilizing advanced diagnostics to provide clinicians with all the data they need to make informed decisions. AST results will ensure only the most appropriate agent is selected, and MIC results allow for the lowest possible dose to be administered. But not all systems are created equal.

Laboratories and healthcare professionals need to be confident in their results, meaning they need industry-leading reliable, validated systems that mimic established reference methods. When it comes to an MIC, they need results based on definitive, observed growth.

Importantly, the best systems will work in harmony with new agents, enabling hospitals to seamlessly introduce them into routine workflows as quickly as possible. Because what is the point of innovative new medicines if patients are unable to access them?

## Our stewardship portfolio

Thermo Fisher Scientific is dedicated to supporting our customers' antimicrobial stewardship efforts and protecting public health. Our AST solutions are fully validated, with gold standard-level accuracy.[11] They provide laboratories with reliable, robust results which may guide clinical decisions.

We are dedicated, in our collaboration with pharmaceutical companies, to developing new antimicrobials and expediting their incorporation into our antimicrobial testing portfolio.

- The Thermo Scientific™ Sensititre™ System, a single integrated AST platform using broth microdilution (BMD) for gold standard AST accuracy, has a flexible workflow that can fit the needs of any laboratory. With more than 300 antimicrobials, including the latest on the market, available on both standard and customizable MIC plates, it allows laboratories to consolidate offline tests while meeting FDA, CLSI, and EUCAST breakpoint requirements.

- The Sensititre System provides a full range of antimicrobial dilutions for guiding more precise clinical decisions.

- Validation studies have shown that AST with Thermo Scientific™ Oxoid™ AST discs provide accurate and reproducible performance, aligning closely with EUCAST and CLSI standards.[12]

- Available in a variety of common and specialized compounds, including cefiderocol, Oxoid AST discs allow you to achieve high quality results backed by over 50 years of experience in disc development and production.

For more information on our complete range of AST solutions and to subscribe to our susceptibility testing, empowered newsletter, **visit thermofisher.com/AST.**

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